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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,880	01/17/2006	Young Shin Song	4240-140	2148
23448 7590 09/03/2008 INTELLECTUAL PROPERTY / TECHNOLOGY LAW PO BOX 14329 RESEARCH TRIANGLE PARK, NC 27709				
EXAMINER JOIKE, MICHELE K				
ART UNIT 1636		PAPER NUMBER		
MAIL DATE 09/03/2008		DELIVERY MODE PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/564,880

**Applicant(s)**

SONG ET AL.

**Examiner**

MICHELE K. JOIKE

**Art Unit**

1636

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 02 June 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) 5-7, 9 and 15-22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4, 8, 10-14 and 23-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 1/17/06 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB-083)
- Paper No(s)/Mail Date 1/17/06
- 4) ☐ Interview Summary (PTO-413)
- Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

***Election/Restrictions***

Applicant's election with traverse of Group I in the reply filed on June 2, 2008 is acknowledged. The traversal is on the ground(s) that Groups I and II are so linked as to form a single inventive concept because the two groups contain vectors with similar properties. Additionally, there is no search burden to search all 25 claims together. This is not found persuasive because first, search burden is not relevant for lack of unity. Second, while the vectors do have similar properties, unity of invention was broken by Jo et al, and the inventions in the two groups do not possess the same special technical feature. The T-vector of group I does not require the pHCE-FOREX vector of group II. Additionally, the pHCE-FOREX vector of group II, requires the use of AspEI sites, which are not required in group I. Thus group I and II are biologically, compositionally and biologically distinct and are capable of supporting individual patents.

The requirement is still deemed proper and is therefore made FINAL.

Claims 5-7, 9 and 15-22 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on June 2, 2008. Claims 1-4, 8, 10-14 and 23-25 are examined.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 8, 10, 12-14 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jo et al in view of Poo et al.

Jo et al (Plasmid 45:37-40, 2001, especially pp. 37-39) teach the development of a T-vector with 3'-thymidine overhangs capable of functional as an expression vector, pNB-T with an XcmI cassette. The pNB-T vector was used to PCR clone a reporter gene GAPDH, using the XcmI sites, and then transformed into E. coli. This procedure is a one-step T-vector cloning procedure. The GAPDH gene was then expressed and produced (see Figure 2). The GAPDH gene was amplified using forward and reverse

primers for PCR. However, they do not teach using a constitutive high-level expression vector, or a pHCE vector.

Poo et al (Biotech. Letters 24: 1185-1189, 2002, specifically pp. 1185-1186) teach a pHCE vector for constitutive high-level expression.

The ordinary skilled artisan, desiring to have a T-vector comprising constitutive high-level expression would have been motivated to combine the teachings of Jo et al teaching the development of a T-vector with 3'-thymidine overhangs capable of functional as an expression vector, pNB-T with an XcmI cassette with the teachings of Poo et al, teaching the pHCE vector because Poo et al state that the pHCE system produces twice the amount of protein over the pET vector system. It would have been obvious to one of ordinary skill in the art to use pHCE because Poo et al teach that the vector contains the constitutive promoter, HCE, and constitutive promoters facilitate high-level expression of foreign proteins without induction. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 11-12 and 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jo et al and Poo et al as applied to claims 1-4, 8, 10, 12-14 and 23 above, and further in view of Rowe et al and Velterop et al.

Jo et al teach all of the limitations as described above. However, they do not teach the expression vector with a gene as a PCR product amplified using primers having the amino terminal end of ATG, and a primer specific to the base sequence of the gene.

Poo et al teach all of the limitations described above. However, they do not teach the expression vector with a gene as a PCR product amplified using primers having the amino terminal end of ATG, and a primer specific to the base sequence of the gene.

Rowe et al (Gene 216(1):215-23, 1998, especially fig. 2) teach an integrative vector (pCJR24) constructed for use in the erythromycin producer *Saccharopolyspora erythraea* and in other actinomycetes. It includes the pathway-specific activator gene *actII-ORF4* from the actinorhodin biosynthetic gene cluster of *Streptomyces coelicolor*. The *actI* promoter and the associated ribosome binding site are located upstream of an *NdeI* site (5'-CATATG-3') which encompasses the *actI* start codon. Construction of the expression vector pCJR24 was as follows: A 970-bp DNA fragment (containing the *actII-ORF4* activator gene) was amplified using PCR from pMF1015 using primers which introduced a flanking *SpeI* restriction site upstream of the gene and an *AflII* site downstream. This fragment was introduced into *AatII*-digested and end-repaired pUC19 to yield pCJR18. A 215-bp DNA fragment (containing the bidirectional promoter pair  $P_{actIII}/P_{actI}$ ) was amplified from pMV400 using synthetic primers which introduced an *AflII* site suitably positioned to serve as the start codon for genes to be expressed from  $P_{actIII}$  and an *NdeI* site suitably positioned for expression of genes from  $P_{actI}$ . This PCR

product was digested with *Afl*III and *Nde*I and cloned into pCJR18 previously digested with *Afl*III and *Nde*I to generate pCJR19. A 1.1-kb *Hind*III–*Sph*I fragment containing the *tsr* gene was amplified from pIJ922 introducing the flanking sites in the primers. This fragment was digested with *Hind*III and *Sph*I and introduced into similarly digested pCJR19 to give pCJR24. Therefore, the expression vector contains a gene as a PCR product amplified using primers having the amino terminal end of ATG, and a primer specific to the base sequence of the gene.

Velterop et al (Gene 153(1):63-5, 1995, specifically p. 63) teach a vector for use in transforming *E. coli* containing an *Nde*I site.

The ordinary skilled artisan, desiring to have an expression vector with a gene as a PCR product amplified using primers having the amino terminal end of ATG, and a primer specific to the base sequence of the gene would have been motivated to combine the teachings of Jo et al teaching the development of a T-vector with 3'-thymidine overhangs capable of functional as an expression vector, pNB-T with an *Xcm*I cassette with the teachings of Poo et al, teaching the pHCE vector, with Rowe et al teaching an expression vector with a gene as a PCR product amplified using primers having the amino terminal end of ATG, and a primer specific to the base sequence of the gene, with Velterop et al teaching a vector for use in transforming *E. coli* containing an *Nde*I site because Velterop et al teach that the *Nde*I site permits cloning of a gene at its translation start point without altering the amino-acid sequence of the synthesized protein. It would have been obvious to one of ordinary skill in the art because Velterop et al teach that an altered second amino acid is avoided by using an *Nde*I site. Given

the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

***Allowable Subject Matter***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELE K. JOIKE whose telephone number is (571)272-5915. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michele K Joiike, Ph.D./

Michele K Joiike, Ph.D.  
Examiner  
Art Unit 1636